

EVOLUTIONARY BIOLOGY

Face of the past reconstructed

David M. Lambert and Leon Huynen

DNA is particularly well preserved in hair — enabling the genome of a human to be sequenced, and his ancestry and appearance to be determined, from 4,000-year-old remains.

The impact of the Human Genome Project (HGP)¹ and the development of ‘mega-DNA sequencers’ continue to have ramifications in diverse fields. An excellent example is reported on page 757 of this issue by Rasmussen *et al.*², who describe the first genome sequence of an ancient human. Their work was made possible only by the technical advances seen since the HGP. The authors used bioinformatics tools, databases and molecular-biology techniques to uncover a great deal of information about this ancient person.

Rasmussen *et al.*² recovered DNA from a tuft of 4,000-year-old human hair preserved in permafrost at Qeqertasussuk, Greenland. The hair came from an individual from the Saqqaq culture, the first culture known to inhabit Greenland. On the basis of their DNA analysis, the authors identified the individual as a male. They also determined that, surprisingly, the geographical origin of the man was eastern Siberia, thereby providing insights into the peopling of the New World. Finally, the authors reconstructed some of the features and characteristics of this individual. We predict that many future studies will also combine methods for analysing ancient DNA with the scientific tools and genomic information that have accumulated as a result of the HGP. Such studies have the potential to reconstruct not only our genetic and geographical origins, but also what our ancestors looked like.

DNA analyses of ancient humans and their ancestors have always been technically challenging, from the initial work on an Egyptian mummy³ to the more recent sequencing of Neanderthal DNA⁴. Typically, these studies have been conducted on bone or skin tissue. The main difficulty with such work is that almost all excavated ancient tissues are contaminated with modern human DNA, not to mention substantial numbers of fungal and bacterial colonies^{4–6}. Several measures can be taken to enrich ancient human DNA, such as taking multiple samples of the same specimen, or analysing only short DNA fragments that have the characteristic damage associated with ancient genetic material^{5,6}.

Studies on mammoths⁷, however, show that DNA in hair is typically preserved with little

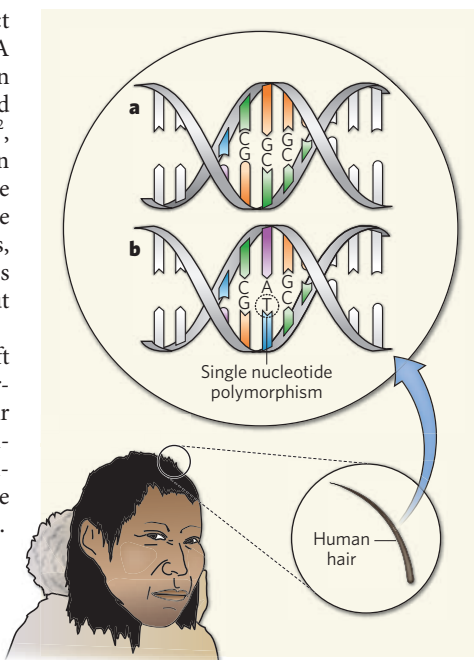


Figure 1 | Single nucleotide polymorphisms of an ancient genome. Rasmussen *et al.*² have sequenced the genome of a man from the Saqqaq culture, using DNA from hair preserved in permafrost in Greenland. They analysed the genome to find single nucleotide polymorphisms (SNPs) — differences in single DNA base pairs that exist between individual genomes, and that may act as markers of an individual's physical traits. **a**, Here, a short stretch of human DNA is shown that is a marker for normal earwax. **b**, In the analogous DNA from the Saqqaq individual, there is a SNP in which a C in the lower strand has been replaced by a T (C, G, T and A denote the four kinds of DNA base). This SNP shows that the Saqqaq man had dry earwax. Rasmussen and colleagues identified other SNPs indicating that the ancient human had, among other things, brown eyes, non-white skin, thick dark hair and an increased susceptibility to baldness.

contamination from fungi or bacteria. Rasmussen *et al.*² therefore extracted the DNA from the Saqqaq specimen in the expectation that it would have retained mostly human DNA. Sure enough, they found that more than 84% of it came from the ancient human. They then

used the latest ‘next-generation’ sequencing technology to generate 20× coverage of most of the ancient genome (79% of the genome was sequenced 20 times; the genome consists of 3 billion base pairs). This is impressive, given that the gold standard for the HGP was 10× coverage.

The authors' next step was to study the genome's single nucleotide polymorphisms (SNPs) — differences at single DNA base pairs that exist between individuals (Fig. 1). These genetic markers are spread relatively uniformly across the human genome, and can provide, among other data, information on the geographical origin of an individual. Such data are especially useful in this instance², because the origin of the Saqqaq culture has been hotly debated. Most theories propose that the Saqqaqs' ancestors were migrants from neighbouring Native American populations, such as the Na-Dene of North America or the Inuit of the New World Arctic.

Rasmussen *et al.*² analysed more than 350,000 SNPs from the ancient genome, comparing them with SNP data of people from several surrounding populations to pinpoint the geographical origin of the Saqqaq individual. Surprisingly, the ancient eskimo proved to be most closely related to three Old World Arctic populations: the Nganasans, Koryaks and Chukchis of the Siberian far east. This suggests that there was a substantial and relatively recent migration across the Bering Strait and over North America to Greenland (see Fig. 3a on page 761). The authors' analysis indicates that the Saqqaqs diverged from the Chukchis about 200 generations (5,400 years) ago, implying that the ancestral Saqqaqs separated from their Old World relatives almost immediately before their migration to the New World.

Human SNPs are now known to number in the millions, and many of them have been identified as reliable markers for an individual's phenotype (characteristics)⁸. Rasmussen *et al.*² used DNA databases to match large numbers of their Saqqaq individual's SNPs to the likely phenotypes of individuals in modern human populations that carry the same SNPs. In this way, the authors were able to provide a wealth of information on their subject's morphology,

V. WARD, UNIV. AUCKLAND



50 YEARS AGO

In his first lecture, Prof. Medawar had emphasized the fallibility and limitations of our efforts to predict the future. Nevertheless, he maintained in his second lecture that it is not true to say that advances in medicine and hygiene must cause a genetical deterioration of mankind; there is more to be feared from a slow decline of human intelligence. But if that is happening, it is because the rather stupid are biologically fitter than those who are innately more intelligent, not because medicine is striving to raise the biological fitness of those people who might otherwise be hopelessly unfit ... Lord Adrian, too, emphasizes the need for much more information ... We have succeeded so well, he observes, in our aim at keeping alive every child that is born that we are certainly preserving many unfavourable genes which would otherwise have died out. "If we set out to save the unfit we must expect more unfitness in the world and more inheritance of the factors which promote it. Even if the radiation level remains as it now is, the advance of science can harm the genetic constitution of the race".

From *Nature* 13 February 1960.

100 YEARS AGO

It is now an evident fact that Paris has recently suffered the ravages of an inundation greater and more severe than any which have visited the city within the last two and a half centuries. A gauge at the bridge of La Tournelle shows the surface of the water as having reached a height above the bed of the river of 27 feet 10½ inches. Normally, it is only about 8 or 9 feet, and it is necessary to go back so far as the year 1658 in order to find any record exceeding, or even approaching, this figure. At that date the height attained was 28 feet 10½ inches ... The causes of the flood are not quite so obvious as the effects.

From *Nature* 10 February 1910.

metabolism and a likely predisposition (Fig. 1). They determined that their individual was an inbred male with a pattern of population-defining SNPs commonly found among east Siberians, and that he had an A+ blood group, brown eyes, non-white skin, thick dark hair and 'shovel-graded' front teeth typical of Asian and Native American populations. What's more, he had an increased susceptibility to baldness, dry earwax and a metabolism and body-mass index commonly found in those who live in cold climates.

With a growing number of SNPs being linked to morphological or physiological characteristics^{9–11}, we have an increasingly powerful forensic tool with which to 'reconstruct' extinct humans and the demographics of populations. This will also allow high-resolution analyses of worldwide population movements, on a scale not previously seen: future studies will probably be able to track movements more broadly across both space and time.

But it won't all be plain sailing. One big problem is that the majority of ancient human remains are found in temperate and even hot environments. Because the rate of degradation of ancient DNA increases exponentially with

temperature, it remains to be seen whether genomic studies of hominin specimens from these regions will recover sufficient DNA to be informative. Whatever the case, Rasmussen and colleagues' findings⁹ will no doubt stimulate a series of additional studies and provide useful methods for future investigations of human evolution.

David M. Lambert and Leon Huynen are in the School of Environment and the School of Biomolecular and Physical Sciences, Griffith University, Nathan, Queensland 4111, Australia.

e-mails: d.lambert@griffith.edu.au;

l.huynen@griffith.edu.au

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NUCLEAR PHYSICS

Weighing up the superheavies

Georg Bollen

To discover superheavy elements and study their properties, we need to know the masses of the isotopes of elements heavier than uranium. Weighing these isotopes in an electromagnetic trap has now become possible.

Nuclear reactions allow us to create elements beyond uranium (element 92), the heaviest element in nature. However, we are far from knowing what the heaviest possible element is. In the sparsely explored territory of superheavy elements, an 'island of stability' is expected. This island would consist of isotopes of elements that are more strongly bound and longer-lived than the isotopes surrounding it. Challenging expeditions towards the island have so far led to the discovery of elements up to element 118. But knowing the masses of the isotopes of elements heavier than uranium (trans-uranium elements) is of great importance for the success of the journey. In this issue (page 785), Block and colleagues¹ describe the first-ever direct measurement of the masses of isotopes of a trans-uranium element. They have used an ion trap as a high-precision scale for weighing isotopes of nobelium, an element that has ten more protons than uranium.

Chemical elements are sorted into a periodic table according to their properties. These properties reflect an atom's electronic structure, which is determined by the number of

protons in the atomic nucleus. In a similar way, the approximately 3,000 known isotopes of the different elements are depicted in a proton number–neutron number diagram, the chart of nuclides. Most of these isotopes are radioactive and can be produced only artificially by using nuclear reactions. In exploring the limits to the existence of nuclides, physicists' expeditions have reached beyond uranium (92 protons) towards the northeast end of the chart of nuclides.

The existence of superheavy elements possessing many more protons than uranium was predicted four decades ago. Their increased stability against nuclear fission would originate from their nuclear shells being filled by protons and neutrons, like the electron orbits in an atom. For certain combinations of numbers of protons and neutrons — 'magic numbers' — a more strongly bound system would be formed that would also have a longer half-life. Accordingly, the superheavy elements are predicted to populate an island of stability located around proton number 120 and neutron number 184 (see Fig. 3 on page 787). Several exploratory groups have set sail^{2–5} for this destination, and